

**REMARKS**

Reconsideration of the this application in light of the above-amendments and following remarks is respectfully requested. Claims 1-11 are currently pending in this application. Applicants confirm the previous election, without traverse, of the species rheumatoid arthritis, stressor of above body temperature and electromagnetic emission and oxidative environment and TNFR:Fc.

**Amendments**

1. Substitute Specification

A substitute specification with the specification and claims in permanent ink is submitted herewith. No new matter has been added to the specification. Additionally, no amendments were made to the specification previous to the submission of this Reply. Accordingly, a copy of the specification as originally filed is submitted.

2. Title

The title has been objected to as not descriptive. The title has been amended to indicate the invention to which the claims are directed.

3. Cross Reference to Related Applications

The Cross Reference to Related Applications has been inserted at the beginning of the specification as required.

4. Claims

Claim 6 has been amended to recite the recommended Markush language. No new matter has been added by this amendment.

5. Abstract

The abstract has been objected to as not descriptive. The abstract has been amended to describe the invention to which the claims are directed. No new matter has been added by this amendment.

Formal Drawings

Formal drawings will be submitted in a supplementary reply.

Corrected Information Disclosure Statement

A corrected IDS and PTO form 1449 is submitted herewith to provide the full citation of the Genetic Engineering News and European Journal of Pharmacology articles. The undersigned is researching the citation for the "Treatment Schedule" and will submit this information to the Office as soon as it is received.

Rejection Under 35 U.S.C. §103(a)

Claims 1-11 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Bolton, USP 5,980,954 (Bolton) in view of Jacobs et. al, USP 5,605,690 (Jacobs). This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met.

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the combined prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. It is well established law that some objective teaching in the prior art or knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. *See, e.g., In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Further, the requisite motivation must come from the prior art, not from the applicant's specification. *See, e.g., In re Dow Chem. Co. v. American Cyanamid Co.*, 5 U.S.P.Q.2d 1529, 1531-32 (Fed. Cir. 1988) ("(t)here must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure.").

The Office Action states that Jacobs teaches a method of lowering the levels of active TNF $\alpha$  in a mammal having arthritis by administering a TNF antagonist, including TNFR:Fc. Additionally, in Example 4, Jacobs teaches that a combination therapy of TNFR:Fc and recombinant murine soluble IL-1 receptor (rm IL-1R) was effective in

suppressing the effects of antigen-induced arthritis in rats. Jacobs does not disclose or describe that the TNF antagonist treatment would be useful in combination with any other kinds of therapies, namely therapies which avoid the long-term use of drugs or those which have been shown to be effective to prevent the onset of autoimmune diseases.

As noted in the specification at page 3, second and third paragraph, treatment with recombinant TNF receptors include recombinant human TNF receptor p55 Fc fusion protein (p55 TNFR:Fc) and recombinant human TNF receptor p75 Fc fusion protein (p75 TNFR:Fc). Both p55 and p75 TNFR:Fc bind to soluble TNF present in the synovial fluid of a patient suffering from rheumatoid arthritis thereby reducing its inflammatory action and resulting in a significant reduction in joint tenderness and swelling. This treatment is typically administered to patients after the onset of rheumatoid arthritis, and may provide some degree of relief from the symptoms associated with the disease. Once treatment with these proteins is discontinued, the symptoms of rheumatoid arthritis typically reappear. Accordingly, this kind of treatment fails to address the underlying cause of rheumatoid arthritis, which is an inappropriate immune response.

The Office Action states that Bolton teaches a method of treating a subject suffering from rheumatoid arthritis by administering autologous blood exposed to an oxidative environment, electromagnetic emission and a temperature above body temperature. Bolton does not disclose or suggest the use of any additional therapies or combining therapies to treat the diseases disclosed, in particular rheumatoid arthritis. Further, without the disclosure or suggestion of the use of additional therapies or combining therapies, there is no indication that doing so would be successful.

It is submitted that a *prima facie* case of obviousness has not been established.

There is no motivation in either Jacobs or Bolton to combine these references to produce the claimed invention, nor is there a reasonable expectation of success combining the references. While the Office Action states that each treatment works individually, there is no suggestion in either document to combine the therapies to produce the claimed invention. Accordingly, it is submitted that this rejection is in error and Applicant's respectfully request that it be withdrawn.

Conclusion

It is submitted that this application is in condition for allowance. Early notice to that effect is respectfully requested.

Respectfully submitted,

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**MARKED UP VERSION SHOWING AMENDMENTS**

**In the Title:**

Method for Treating [Combination Therapy for] Autoimmune and Alloimmune Diseases

**In the Abstract:**

Disclosed is a method [A combination therapy] for treating a mammalian subject suffering from an autoimmune or alloimmune disease by administering to the subject a drug treatment which results in at least partial remission of one or more symptoms of the autoimmune or alloimmune disease, and administering to the subject autologous mammalian blood which has been modified extracorporeally by exposure to at least one stressor selected from an oxidative environment, an electromagnetic emission and a temperature above or below body temperature. The modified mammalian blood is administered to the subject in an amount which is sufficient to maintain the remission of the symptoms of the autoimmune or alloimmune disease.

**In the Claims:**

6. (Amended) The method of claim 5, wherein said recombinant TNF receptor is selected from the group [comprising] consisting of recombinant human TNF receptor p55 Fc fusion protein (p55 TNFR:Fc) and recombinant human TNF receptor p75 Fc fusion protein (p75 TNFR:Fc).